



SEQUENCE LISTING

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Kumar, Shankar

<120> Amphiregulin Antibodies and Their Use to Treat Cancer and
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<210> 1
<211> 252
<212> PRT
<213> Homo sapiens

<400> 1

Met Arg Ala Pro Leu Leu Pro Pro Ala Pro Val Val Leu Ser Leu Leu
1 5 10 15

Ile Leu Gly Ser Gly His Tyr Ala Ala Gly Leu Asp Leu Asn Asp Thr
20 25 30

Tyr Ser Gly Lys Arg Glu Pro Phe Ser Gly Asp His Ser Ala Asp Gly
35 40 45

Phe Glu Val Thr Ser Arg Ser Glu Met Ser Ser Gly Ser Glu Ile Ser
50 55 60

Pro Val Ser Glu Met Pro Ser Ser Ser Glu Pro Ser Ser Gly Ala Asp
65 70 75 80

Tyr Asp Tyr Ser Glu Glu Tyr Asp Asn Glu Pro Gln Ile Pro Gly Tyr
85 90 95

Ile Val Asp Asp Ser Val Arg Val Glu Gln Val Val Lys Pro Pro Gln

100 105 110
 Asn Lys Thr Glu Ser Glu Asn Thr Ser Asp Lys Pro Lys Arg Lys Lys
 115 120 125
 Lys Gly Gly Lys Asn Gly Lys Asn Arg Arg Asn Arg Lys Lys Lys Asn
 130 135 140
 Pro Cys Asn Ala Glu Phe Gln Asn Phe Cys Ile His Gly Glu Cys Lys
 145 150 155 160
 Tyr Ile Glu His Leu Glu Ala Val Thr Cys Lys Cys Gln Gln Glu Tyr
 165 170 175
 Phe Gly Glu Arg Cys Gly Glu Lys Ser Met Lys Thr His Ser Met Ile
 180 185 190
 Asp Ser Ser Leu Ser Lys Ile Ala Leu Ala Ala Ile Ala Ala Phe Met
 195 200 205
 Ser Ala Val Ile Leu Thr Ala Val Ala Val Ile Thr Val Gln Leu Arg
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 Arg Gln Tyr Val Arg Lys Tyr Glu Gly Glu Ala Glu Glu Arg Lys Lys
 225 230 235 240
 Leu Arg Gln Glu Asn Gly Asn Val His Ala Ile Ala
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 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr
 20 25 30
 Asn Met Tyr Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
 35 40 45

Gly Tyr Ile Asp Pro Tyr Tyr Gly Asp Pro Gly Tyr Ser Gln Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met His Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Arg Gly Asn Phe Pro Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Thr Leu Thr Val Ser Ser
 115

<210> 3
 <211> 107
 <212> PRT
 <213> Mus sp.

<400> 3

Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
 1 5 10 15

Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
 20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
 35 40 45

Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr
 65 70 75 80

Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Tyr
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

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<211> 116
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 <213> Mus sp.

<400> 4

Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Ser Gly Ala
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Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Tyr
 20 25 30

Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Cys Ile Asp Pro Glu Asn Gly Asp Thr Glu Tyr Ala Pro Asn Phe
 50 55 60

Gln Gly Arg Ala Thr Met Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
 65 70 75 80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Tyr Gly Gly Thr Ile Thr Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val
 100 105 110

Thr Val Ser Ala
 115

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Gln Ala Val Val Thr Gln Glu Ser Ala Leu Thr Thr Ser Pro Gly Glu
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 20 25 30

Asn Ser Ala Asn Trp Val Gln Glu Lys Pro Asp His Leu Phe Thr Gly
 35 40 45

Leu Ile Gly Gly Thr Ile Asn Arg Val Pro Gly Val Pro Ala Arg Phe
 50 55 60

Ser Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala
 65 70 75 80

Gln Thr Glu Asp Glu Ala Ile Tyr Phe Cys Ala Leu Trp Tyr Ser Asn
 85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
 100 105 110

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<210> 8
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 tgcaaggctt ctgggttatgc attcactaac tacaacatgt actgggtgaa gcagagccat 180
 ggaaagagcc ttgagtggat tggatatatt gatccttact atggtgatcc tggctacagc 240
 cagaagttca agggcaaggc cacattgact gttgacaagt cctccagcac agcctacatg 300
 catctcaaca gcctgacatc tgaggactct gcagtctatt actgtgcaag acggggtaac 360

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Met Glu Trp Arg Trp Ile Phe Leu Phe Leu Leu Ser Gly Thr Thr Gly
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Val His Ser Glu Ile Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys
 20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe
 35 40 45

Thr Asn Tyr Asn Met Tyr Trp Val Lys Gln Ser His Gly Lys Ser Leu
 50 55 60

Glu Trp Ile Gly Tyr Ile Asp Pro Tyr Tyr Gly Asp Pro Gly Tyr Ser
 65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
 85 90 95

Thr Ala Tyr Met His Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
 100 105 110

Tyr Tyr Cys Ala Arg Arg Gly Asn Phe Pro Tyr Tyr Phe Asp Tyr Trp
 115 120 125

Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
 130 135

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gacatcaaga tgacccagtc tccatcttcc atgtatgcat ctctaggaga gagagtcact 120

atcacttgca aggcgagtca ggacattaat agctatttaa gctgggtcca gcagaaacca 180
 gggaaatctc ctaagaccct gatctatcgt gcaaacagat tggtagatgg ggtcccatca 240
 aggttcagtg gcagtggatc tgggcaagat tattctctca ccatcagcag cctggagtat 300
 gaagatatgg gaatttatta ttgtctacag tatgatgagt ttccgtacac gtccggaggg 360
 gggaccaagc tggaaataaa a 381

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<400> 11

Met Arg Thr Pro Ala Gln Phe Leu Gly Ile Leu Leu Leu Trp Phe Pro
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Gly Ile Lys Cys Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr
 20 25 30

Ala Ser Leu Gly Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp
 35 40 45

Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro
 50 55 60

Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser
 85 90 95

Ser Leu Glu Tyr Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp
 100 105 110

Glu Phe Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 115 120 125

<210> 12
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 <213> Artificial

<220>
 <223> humanized antibody

<400> 12

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1 5 10 15

Ser Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

Asn Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asp Pro Tyr Tyr Gly Asp Pro Gly Tyr Ser Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Asn Phe Pro Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
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<213> Homo sapiens

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<223> Xaa can be any naturally occurring amino acid

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<221> MISC_FEATURE

<222> (99)..(108)

<223> Xaa can be any naturally occurring amino acid

<400> 13

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Thr Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Thr Phe Thr Xaa Xaa
 20 25 30

Xaa Xaa Xaa Trp Val Gln Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45

Gly Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 50 55 60

Xaa Xaa Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Asp Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Thr Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Trp Gly Gln Gly
 100 105 110

Thr Leu Val Thr Val Ser Ser
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<210> 14
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<220>
 <223> humanized antibody

<400> 14

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
 20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Thr Leu Ile
 35 40 45

Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Gln Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Tyr
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 15
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 <212> PRT
 <213> Homo sapiens

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 <223> Xaa can be any naturally occurring amino acid

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 <223> Xaa can be any naturally occurring amino acid

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 <223> Xaa can be any naturally occurring amino acid

<400> 15

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 20 25 30

Xaa Xaa Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
 35 40 45

Tyr Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 85 90 95

Xaa Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 16
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 <212> DNA
 <213> Artificial

<220>
 <223> humanized antibody

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 tccactctga ggtccagctg gtgcagtctg gagctgaggt gaagaagcct ggggcttctg 120
 tgaaaatatc ctgcaagggt tctgggttat cattcactaa ctacaacatg tattgggtga 180
 ggcaggcccc tggaaagggc cttgagtgga ttggatatat tgatccttac tatggtgate 240
 ctggctacag ccagaagttc aagggcaagg ccacattgac tgttgacaag tccaccagca 300
 cagcctacat ggagctcagc agcctgaggt ctgaggacac tgcagtctat tactgtgcaa 360
 gacgtggcaa cttcccgtag tactttgact actggggcca aggcaccctt gtcacagtct 420
 catcaggtga gtcttcacaa cctctaga 448

<210> 17
 <211> 138
 <212> PRT
 <213> Artificial

<220>
 <223> humanized antibody

<400> 17

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 1 5 10 15

Val His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
 20 25 30

Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Ala Phe
 35 40 45

Thr Asn Tyr Asn Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu

50

55

60

Glu Trp Ile Gly Tyr Ile Asp Pro Tyr Tyr Gly Asp Pro Gly Tyr Ser
65 70 75 80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Thr Ser
85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Arg Arg Gly Asn Phe Pro Tyr Tyr Phe Asp Tyr Trp
115 120 125

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
130 135

<210> 18
<211> 415
<212> DNA
<213> Artificial

<220>
<223> humanized antibody

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gtatcaaagtg tgacatccag atgacccagt ctccatcttc cctgtctgca tctgttgagg 120
acagggtcac tatcacttgc aaagcaagtc aggacattaa tagctattta agctgggtcc 180
agcagaaacc agggaaagct cctaagaccc tgatctatcg tgcaaacaga ttggtagatg 240
gggtcccatc aagattcagt ggcagtggat ctgggcaaga ttatactctc accatcagta 300
gcctgcagcc tgaggatttc gcaacttatt attgtctaca gtatgatgag tttccgtaca 360
cgttcggagg agggaccaag gtggaaataa aacgtaagtg cactttcctt ctaga 415

<210> 19
<211> 127
<212> PRT
<213> Artificial

<220>
<223> humanized antibody

<400> 19

Met Arg Thr Pro Ala Gln Phe Leu Gly Ile Leu Leu Leu Trp Phe Pro
 1 5 10 15

Gly Ile Lys Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
 20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp
 35 40 45

Ile Asn Ser Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro
 50 55 60

Lys Thr Leu Ile Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Gln Asp Tyr Thr Leu Thr Ile Ser
 85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Tyr Asp
 100 105 110

Glu Phe Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 115 120 125

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 <211> 75
 <212> DNA
 <213> Artificial

<220>
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 caggtgtcca ctctg 75

<210> 21
 <211> 77
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 21
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tggaacacctg tagttcc

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<210> 22
 <211> 75
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 22
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 aacatgtatt ggggtg 75

<210> 23
 <211> 79
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

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 caatacatgt tgtagttag 79

<210> 24
 <211> 68
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 24
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 acattgac 68

<210> 25
 <211> 80
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 25
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 tcaatgtggc cttgcccttg 80

<210> 26
 <211> 79
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 26
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 actactttga ctactgggg 79

<210> 27
 <211> 79
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 27
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 cagtagtcaa agtagtacg 79

<210> 28
 <211> 20
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 28
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<210> 29
 <211> 21
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 29
 gactcgtcta gaggttgtga g 21

<210> 30
 <211> 71
 <212> DNA

<213> Artificial

<220>

<223> oligonucleotide

<400> 30

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<211> 74

<212> DNA

<213> Artificial

<220>

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gaaaccagag caac 74

<210> 32

<211> 68

<212> DNA

<213> Artificial

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ttaatagc 68

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<211> 72

<212> DNA

<213> Artificial

<220>

<223> oligonucleotide

<400> 33

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gtcctgactt gc 72

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<211> 78

<212> DNA

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<220>
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<400> 34
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 attcagtggc agtggatc 78

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<220>
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 atcttg 66

<210> 36
 <211> 75
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 36
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 gtacacgttc ggagg 75

<210> 37
 <211> 72
 <212> DNA
 <213> Artificial

<220>
 <223> oligonucleotide

<400> 37
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 gtgtacggaa ac 72

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<220>

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<400> 38

ctagccacgc gtccaccatg

20

<210> 39

<211> 19

<212> DNA

<213> Artificial

<220>

<223> oligonucleotide

<400> 39

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19